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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/734,149	12/15/2003	Michael H. Julius	32388-2038	2082

33721 7590 10/12/2005

TORYS LLP
79 WELLINGTON ST. WEST
SUITE 3000
TORONTO, ON M5K 1N2
CANADA

EXAMINER	
BELYAVSKYI, MICHAIL A	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 10/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/734,149	JULIUS ET AL.	
	Examiner	Art Unit	
	Michail A. Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-14,16 and 33-62* is/are pending in the application.

4a) Of the above claim(s) *41,42,52,53 and 61* is/are withdrawn from consideration.

5)☒ Claim(s) *40,51 and 60* is/are allowed.

6)☒ Claim(s) *10-14,16,33-39,43-50 and 54-59* is/are rejected.

7)☒ Claim(s) *62* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 07/15/05 is acknowledged.

Claims 10-14, 16 and 33-62 are pending.

2. Applicant's election of group IV, claims 16-19, 21 and 23, now claims 10-14, 16, 33-40, 43-51, 54-60 in the reply filed on 07/15/05 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 41, 42, 52, 53, and 61 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Claims 10-14, 16, 33-40, 43-51 and 54-60 and 62 as they read on a method of vaccinating a patient comprising administering an antigen other than CD14 and a polypeptide, wherein said polypeptide is encoded by a nucleotide sequence that has at least 62.6 % identity with SEQ ID NO:1 and that hybridizes thereto under high stringency conditions wherein said polypeptide includes the amino acid sequence of SEQ ID NO:4 are under consideration in the instant application.

3. The specification is objected to under 37 CFR 1.821(d) for failing to disclose SEQ ID NOS, for the amino acid sequence disclosed on page 28, line 1.

4. The specification on page 1, paragraph 1 should be amended to reflect the status of the parent 09/313177 application.

5. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention *to which the claims are directed.*

6. Applicant is advised that should claim 60 be found allowable, claim 62 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

7. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claim 54 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Dependent claim 54 recites "said polypeptide vaccine" second line. There is insufficient antecedent basis for this limitation in the claims, since base Claim 16 does not recite "polypeptide vaccine".

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11 . Claims 10-14, 16, 33-39, 43-50 and 54-59 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a New Matter rejection**.

" wherein said polypeptide is encoded by a nucleotide sequence that has at least 62.6 % identity with SEQ ID NO:1 and that hybridizes thereto under high stringency conditions which include a wash step in 0.1 ssc,1%SDS at 65^0C for 3 hours" claimed in claim 16 represent(s) a departure from the specification and the claims as originally filed. The passages pointed by the applicant do not provide a clear support for "wherein said polypeptide is encoded by a nucleotide sequence that has at least 62.6 % identity with SEQ ID NO:1 and that hybridizes thereto under high stringency conditions which include a wash step in 0.1 ssc,1%SDS at 65^0C for 3 hours" . The specification and the claims as originally field only support " a polypeptide having the amino acid sequence identified as SEQ ID NO: 4, SEQ ID NO:5 or SEQ ID NO:6, a conservatively substituted variant thereof, a fragment of said sequence or a conservatively substituted variant of said fragment which activates mammalian B cells".

12. Claims 10-14, 16, 33-39, 43-50 and 54-59 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of vaccinating a patient comprising administering an antigen other than CD14 and a polypeptide, wherein said polypeptide has an amino acid sequence of SEQ ID NO:4 , SEQ ID NO:5 or SEQ ID NO: 6; or wherein said antigen and polypeptide of SEQ ID NO:4 , SEQ ID NO:5 or SEQ ID NO: 6 are conjugated to each other or provided in a kit for preparation of a vaccination does not reasonably provide enablement for: (i) a method of vaccinating a patient comprising administering an antigen other than CD14 and a polypeptide, wherein said polypeptide is encoded by a nucleotide sequence that has at least 62.6 % or 74.2 % identity with SEQ ID NO:1 and that hybridizes thereto under high stringency conditions, as claimed in claims 16 and 33; or (ii) wherein the polypeptide includes *any* conservative substituted variant of SEQ ID NO:4 , SEQ ID NO:5 and SEQ ID NO: 6 , or comprising any fragment of said sequences or any conservatively substituted variant of said fragment which activates mammalian B cells, claimed in claims 34 –39; or (iii) wherein the antigen and the polypeptide, wherein said polypeptide is encoded by a nucleotide sequence that has at least 62.6 % or 74.2 % identity with SEQ ID NO:1, are conjugated to each other, claimed in claims 43 and 44; or (iv) wherein the antigen and the polypeptide, wherein said polypeptide includes *any* conservative substituted variant of SEQ ID NO:4 , SEQ ID NO:5 and SEQ ID NO: 6 , or any fragment of said sequences or any conservatively substituted variant of said fragment which activates mammalian B cells, are conjugated to each other claimed in claims 45-50; or (v) further comprising a step of mixing the antigen and said polypeptide prior to administering claimed in claim 54, or (vi) wherein a polypeptide is recombinant or administering in combination with a pharmaceutical excipient, claimed in claims 55-56, or wherein the polypeptide or any variant thereof and a antigen are provided in a kit for the preparation of a vaccination claimed in claims 10-14 and 57-59 .

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification does not enable one of skill in the art to practice the invention as claimed without undue experimentation.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, limited working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

The claims as written encompass a method of vaccinating a patient, comprising administering an antigen and a genus of polypeptide encoded by a nucleotide sequence that has at least 62.6 % identity with SEQ ID NO:1. The genus encompasses peptides wherein such peptides have numerous differences in amino acid sequences.

A. The Specification disclosed that nucleotide sequence of SEQ ID NO: 1 encoded a bovine polypeptide of SEQ ID NO:4, that is a bovine CD14. The Specification also disclosed a human CD14 of SEQ ID NO:5 , which is encoded by nucleotide sequence of SEQ ID NO:2 and mouse CD14 of SEQ ID NO: 6, which is encoded by nucleotide sequence of SEQ ID NO: 3 (see pages 12 and 13 and FIG. 6 and 7 in particular). The Specification disclosed studies wherein only said CD14 show a capacity to stimulate B cells (see overlapping pages 38-41 in particular).

Applicant has not taught how to make and/or use (i) a method of vaccinating a patient comprising administering an antigen other than CD14 and a polypeptide, wherein said polypeptide is encoded by a nucleotide sequence that has at least 62.6 % or 74.2 % identity with SEQ ID NO:1 and that hybridizes thereto under high stringency conditions, as claimed in claims 16 and 33; or (ii) wherein the polypeptide includes *any* conservative substituted variant of SEQ ID NO:4 , SEQ ID NO:5 and SEQ ID NO: 6 , or comprising any fragment of said sequences or any conservatively substituted variant of said fragment which activates mammalian B cells, claimed in claims 34 –39; or (iii) wherein the antigen and the polypeptide, wherein said polypeptide is encoded by a nucleotide sequence that has at least 62.6 % or 74.2 % identity with SEQ ID NO:1, are conjugated to each other, claimed in claims 43 and 44; or (iv) wherein the antigen and the polypeptide, wherein said polypeptide includes *any* conservative substituted variant of SEQ ID NO:4 , SEQ ID NO:5 and SEQ ID NO: 6 , or any fragment of said sequences or any conservatively substituted variant of said fragment which activates mammalian B cells, are conjugated to each other claimed in claims 45-50; or (v) further comprising a step of mixing the antigen and said polypeptide prior to administering claimed in claim 54, or (vi) wherein a polypeptide is recombinant or administering in combination with a pharmaceutical excipient, claimed in claims 55-56, or wherein the polypeptide or any variant thereof and a antigen are provided in a kit for the preparation of a vaccination claimed in claims 10-14 and 57-59. The structural and functional characteristics of polypeptides encoded by a nucleotide sequence that has at least 62.6 % or 74.2 % identity with SEQ ID NO:1 , a conservatively substituted variant thereof a fragment of said sequences and a conservative substituted variant of said fragment which activates mammalian B cells are not defined in the specification and in the claim. Applicant has not exemplified any *in vitro or in vivo* studies or in animal models wherein *any* polypeptides encoded by a nucleotide sequence that has at least 62.6 % or 74.2 % identity with SEQ ID NO:1 , a conservatively substituted variant thereof a fragment of said sequences and a conservative substituted variant of said fragment can activate mammalian B cells.

Applicant has not provided sufficient biochemical information (e.g. structural characteristics, amino acid composition , physicochemical properties, etc) that distinctly identifies such polypeptides encoded by a nucleotide sequence that has at least 62.6 % or 74.2 % identity with SEQ ID NO:1 , a conservatively substituted variant thereof or comprising a fragment of said sequences and a conservative substituted variant of said fragment other than a bovine CD14 of SEQ ID NO:4, a human CD14 of SEQ ID NO:5 and mouse CD14 of SEQ ID NO: 6. While any "encoded by a nucleotide sequence that has at least 62.6 % or 74.2 % identity with SEQ ID NO:1 , or comprising a conservatively substituted variant thereof a fragment of said sequences and a conservative substituted variant of said fragment " may have some notion to activate B cells, claiming biochemical molecules by such properties fails to provide sufficient guidance and

direction as to how the skilled artisan can make such agents, commensurate in scope with the claimed invention.

Applicant is relying upon certain biological activities and the disclosure of a limited species to support an entire genus. It is well known that minor structural differences among even structurally related compounds or compositions can result in substantially different biology, expression, and pharmacology of proteins. Therefore, structurally unrelated any polypeptide encoded by a nucleotide sequence that has at least 62.6 % or 74.2 % identity with SEQ ID NO:1 , a conservatively substituted variant thereof, or comprising a fragment of said sequences and a conservative substituted variant of said fragment encompassed by the claimed invention other than than a bovine CD14 of SEQ ID NO:4, a human CD14 of SEQ ID NO:5 and mouse CD14 of SEQ ID NO: 6. would be expected to have greater differences in their activities.

Whisstock et al (Quarterly Review of Biophysics, 2003, 36, pp307-340) teaches that prediction of protein function from sequence and structure is difficult problem, because homologous proteins often have different function. A fundamental problem is that function is in many cases an ill-defined concept (see Abstract in particular). Furthermore, the specification fails to teach what deletions, truncations, substitutions and mutations of the disclosed sequence can be tolerated that will allow the protein to function as claimed, i.e. to activate B cells. While it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with reasonable expectation of success are limited. Certain positions in the sequence are critical to the three-dimensional structure/function relationship, and these regions can tolerate only conservative substitutions or no substitutions.

Attwood (Science 2000; 290:471-473) teaches that "[i]t is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences. Similarly, Skolnick et al. (Trends in Biotech. 2000; 18(1):34-39) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Moreover, Whisstock et al (Quarterly Review of Biophysics, 2003, 36, pp307-340) teaches that prediction of protein function from sequence and structure is difficult problem, because homologous proteins often have different function. A fundamental problem is that function is in many cases an ill-defined concept (see Abstract in particular). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2). Finally, even single amino acid differences can result in drastically altered functions between two proteins. For example, Metzler et al. (Nature Structural Biol. 1997; 4:527-531) show that any of a variety of single amino acid changes can alter or abolish the ability of CTLA4 to interact with its ligands CD80 and CD86 (e.g., summarized in Table 2). Thus it is unpredictable if any functional activity will be shared by two polypeptides having less than 100% identity over the full length of their sequences.

In view of this unpredictability the skilled artisan would not reasonably expect a polypeptide encoded by a nucleotide sequence having anything less than 100% identity *over the full length of SEQ ID NO:1* to *share the same function* as the polypeptide encoded by a nucleotide sequence of SEQ ID NO:1. Thus, the recitation of percent identity language, in the absence of limitations regarding the *sequence length over which the percent identity is required*; does not allow the skilled artisan to make and use the encoding nucleic acids commensurate in scope with the instant claims without undue experimentation.

B. Similarly, the fact that two nucleic acid sequences will hybridize under moderate or stringent conditions does not in and of itself require that the two sequences share any functional activity. Thus the same observations apply to the recitation of "nucleotide that hybridizing under stringent condition", claimed in claim 16 as were noted above with respect to "percent identity" language. Further, it was well known in the art at the time the invention was made that hybridization could occur between two sequence based upon short stretches of 100% identity. Thus a great deal of sequence variability *with respect to the full-length nucleic acid* is possible and in the absence of a clear recitation that the identity is over the full length of SEQ ID NO:1, the claim reads on subsequences and would be viewed by the skilled artisan as been even less likely to encode a polypeptide with the same function as polypeptide encoded by SEQ ID NO:4. Thus as for the recitation of percent identity, hybridization language in the absence of limitations regarding both the *hybridization conditions* and the *sequence length over which the hybridization takes place*; does not allow the skilled artisan to make and use the hybridizing nucleic acids commensurate in scope with the instant claims without undue experimentation.

C. Also an issue is that the instant claim language appears to encompass fragments. For example, claims 34 and 35 recites a polypeptide comprising fragment of SEQ ID NO:4, or SEQ ID NO5 or SEQ ID NO:6 or a conservatively substituted variant of said fragment. Such a recitation does not require that the amino acid encode the sequence set forth in SEQ ID NOs: 4-6 but rather encompasses any amino acid sequence comprising either the full length of SEQ ID NOs:4-6 or *any fragment*. However, the specification does not appear to have provided sufficient guidance as to which fragments of SEQ ID NOs:4-6 would share the function of activating mammalian B cells . Neither does the specification appear to have provided any working examples of any functional fragments. Thus it would require undue experimentation of the skilled artisan to determine which fragments of SEQ ID NOs:4-6 would have the function of the SEQ ID NOs: 4-6. In addition , "comprising" is considered open-ended claim language and includes amino acid residues outside of the specified peptide. It means that a peptide may include additional unrecited amino acid on either or both of the N or C-terminus of a given sequence . Therefore, polypeptide "comprising" fragment of SEQ ID NO:4, or SEQ ID NO5 or SEQ ID NO:6 or a conservatively substituted variant of said fragment includes an unlimited number of amino acid sequences "comprising" an unlimited number of polypeptides. The disclosure of SEQ ID NOS: 4-6 cannot support the entire genus of polypeptide comprising" fragment of SEQ ID NO:4, or SEQ ID NO5 or SEQ ID NO:6 or a conservatively substituted variant of said fragment as part of their sequence that can activates mammalian B cells.

Thus, Applicant has not provided sufficient guidance to enable one skill in the art to use claimed (i) a method of vaccinating a patient comprising administering an antigen other than CD14 and a polypeptide, wherein said polypeptide is encoded by a nucleotide sequence that has at least 62.6 % or 74.2 % identity with SEQ ID NO:1 and that hybridizes thereto under high stringency conditions, as claimed in claims 16 and 33; or (ii) wherein the polypeptide includes *any* conservative substituted variant of SEQ ID NO:4 , SEQ ID NO:5 and SEQ ID NO: 6 , or comprising any fragment of said sequences or any conservatively substituted variant of said fragment which activates mammalian B cells, claimed in claims 34 –39; or (iii) wherein the antigen and the polypeptide, wherein said polypeptide is encoded by a nucleotide sequence that has at least 62.6 % or 74.2 % identity with SEQ ID NO:1, are conjugated to each other, claimed in claims 43 and 44; or (iv) wherein the antigen and the polypeptide, wherein said polypeptide includes *any* conservative substituted variant of SEQ ID NO:4 , SEQ ID NO:5 and SEQ ID NO: 6 , or any fragment of said sequences or any conservatively substituted variant of said fragment which activates mammalian B cells, are conjugated to each other claimed in claims 45-50; or (v) further comprising a step of mixing the antigen and said polypeptide prior to administering claimed in claim 54, or (vi) wherein a polypeptide is recombinant or administering in combination with a pharmaceutical excipient, claimed in claims 55-56, or wherein the polypeptide or any variant thereof and a antigen are provided in a kit for the preparation of a vaccination claimed in claims 10-14 and 57-59 in manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

13. Claims 10-14, 16, 33-39, 43-50 and 54-59 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of : a method of vaccinating a patient comprising administering an antigen other than CD14 and a polypeptide, wherein said polypeptide has an amino acid sequence of SEQ ID NO:4 , SEQ ID NO:5 or SEQ ID NO: 6; or wherein said antigen and polypeptide of SEQ ID NO:4 , SEQ ID NO:5 or SEQ ID NO: 6 are conjugated to each other or provided in a kit for preparation of a vaccination.

Applicant is not in possession of : (i) a method of vaccinating a patient comprising administering an antigen other than CD14 and a polypeptide, wherein said polypeptide is encoded by a nucleotide sequence that has at least 62.6 % or 74.2 % identity with SEQ ID NO:1 and that hybridizes thereto under high stringency conditions, as claimed in claims 16 and 33; or (ii) wherein the polypeptide includes *any* conservative substituted variant of SEQ ID NO:4 , SEQ ID NO:5 and SEQ ID NO: 6 , or comprising any fragment of said sequences or any conservatively substituted variant of said fragment which activates mammalian B cells, claimed in claims 34 –39; or (iii) wherein the antigen and the polypeptide, wherein said polypeptide is encoded by a nucleotide sequence that has at least 62.6 % or 74.2 % identity with SEQ ID NO:1, are conjugated to each other, claimed in claims 43 and 44; or (iv) wherein the antigen and the polypeptide, wherein said polypeptide includes *any* conservative substituted variant of SEQ ID NO:4 , SEQ ID NO:5 and SEQ ID NO: 6 , or any fragment of said sequences or any conservatively substituted variant of said fragment which activates mammalian B cells, are conjugated to each other claimed in claims 45-50; or (v) further comprising a step of mixing the antigen and said polypeptide prior to administering claimed in claim 54, or (vi) wherein a polypeptide is recombinant or administering in combination with a pharmaceutical excipient, claimed in claims 55-56, or wherein the polypeptide or any variant thereof and a antigen are provided in a kit for the preparation of a vaccination claimed in claims 10-14 and 57-59.

The claimed invention is drawn to a method of vaccination comprising administering antigen other than CD14 and a genus of polypeptide encoded by a nucleotide sequence that has at least 62.6 % identity with SEQ ID NO:1. The genus of encompasses peptides wherein such peptides have numerous differences in amino acid sequences. There is no evidence that there is any *per se* structure/function relationship between the disclosed a bovine CD14 of SEQ ID NO:4, a human CD14 of SEQ ID NO:5 and mouse CD14 of SEQ ID NO: 6, and any others that might be found using the claimed method. The specification does not disclosed and exemplified any polypeptide, wherein said polypeptide is encoded by a nucleotide sequence that has at least 62.6 % or 74.2 % identity with SEQ ID NO:1 and that hybridizes thereto under high stringency conditions, or includes *any* conservative substituted variant of SEQ ID NO:4 , SEQ ID NO:5 and SEQ ID NO: 6 , or comprising any fragment of said sequences or any conservatively substituted variant of said fragment which activates mammalian B cells and thus can be used in the method of vaccinating a patient.

Applicant has disclosed a limited number of species; therefore, the skilled artisan cannot envision all the contemplated amino acid sequence possibilities recited in the instant claims. Consequently, conception in either case cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. The sequences themselves are required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993). A description of what a material does (i.e. activates B cells) rather than of what it is, usually does not suffice. The patent does not more than describe the desired function of the compound called for and contains no information by which a person of ordinary skill in the art would understand that the inventors possessed the

claimed invention. At best, it simply indicates that one should run tests on a wide spectrum of compounds in the hope that at least one of them will work. Inadequate written description that merely identifies a plan to accomplish an intended result "is an attempt to preempt the future before it has arrived" *Fiers v. Revel*, 984 F.2d 1164,1171 9Fed.Cir. 1993).

A description of a genus of polypeptide sequences may be achieved by means of a recitation of a representative number of polypeptide sequences, defined by amino acid sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. Regents of the University of California v. Eli Lilly&Co., 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Revised Guidelines for the Examination of Patent Applications Under the 35 U.S.C.112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No.4, pages 1099-1111, Friday January 5, 2001.

14. The prior art does not teach or suggest the claimed invention recited in claims 40, 51 and 60.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/272-0840. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/272-0841.

The fax number for the organization where this application or proceeding is assigned is 571/273-8300

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michail Belyavskyi, Ph.D.
Patent Examiner
Technology Center 1600
October 2, 2005